

Remarks

Reconsideration of the application is respectfully requested in view of the following remarks and enclosed Exhibits A and B. Claims 1, 4-9 and 11 were pending. No claims are added or cancelled. Therefore, claims 1, 4-9, and 11 are still pending, with claims 5-9 and 11 withdrawn. Consideration and allowance of the pending claims is requested.

35 U.S.C. § 112, first paragraph

Claims 1 and 4 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants disagree and request reconsideration.

The Office action alleges that the specification fails to present any scientific reasoning as why inhibition of a functional channel (administration of an inhibitor compound) would have the same or similar effect as observed in an animal with a severed genotype (1B knockout mutant mice) and that there are no working examples for administration of at least one inhibitor. Applicants enclose a Rule 132 Declaration (Exhibit A) providing data demonstrating that administration of ω -conotoxin GVIA (an inhibitor of $\alpha 1B$ subunit of N-type calcium channel) can alleviate symptom of depression. The ω -conotoxin GVIA compound was administered to wild-type mice and the effect on depression monitored using a forced swimming test. Support for the methods used is provided throughout the specification, for example at page 11, line 1 – page 13, line 25 and Example 2 starting on page 25. For example, the specification teaches parenteral administration on page 11, line 20 (which includes the local injection methods used in Exhibit A). As noted in the specification (*e.g.*, see page 13, lines 13-19), appropriate dosages can be determined empirically and the decision of effective dosage depends on the administration pathway, etc. and one skilled in the art can decide effective dosage. Further, omega-conotoxin GVIA is a well-known inhibitor of alpha-1B subunit of N-type calcium channel before the priority date of the present application (see Exhibit B; Feng *et al.*, *J. Biol. Chem.* 276:15728-35, 2001). Therefore, the specification provides support for the experiments and results shown in the Rule 132 Declaration.

As shown in the Figure on page 2 of the Rule 132 Declaration, mice administered ω -conotoxin GVIA show significantly reduced immobility as compared to vehicle-treated control

mice. These results demonstrate that the claimed methods work as predicted, namely that an inhibitor of $\alpha 1B$ subunit of N-type calcium channel can be used to treat depression in a subject *in vivo*.

In view of this data, Applicants request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

Conclusion

If any matters remain to be discussed before a Notice of Allowance is issued, the Examiner is respectfully requested to contact the undersigned for a telephone interview at the telephone number listed below.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 595-5300
Facsimile: (503) 595-5301

By /Sheree Lynn Rybak/
Sheree Lynn Rybak, Ph.D.
Registration No. 47,913